

SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following items which are listed on the attached Form PTO-1449 (**Exhibit E**). Items 1-50 are U.S. Patents or U.S. Patent Application Publications. As permitted by 37 C.F.R. 1.98(a)(2)(ii), no copies of these items are included herewith. Copies of items 51-145 are attached hereto as Exhibits 1-94, respectively.

1. U.S. Patent No. 4,824,775, issued April 25, 1989, Dattagupta;
2. U.S. Patent No. 5,118,605, issued June 2, 1992, Urdea;
3. U.S. Patent No. 5,174,962, issued March 3, 1999, Ju;
4. U.S. Patent No. 5,302,509, issued December 4, 1994, Cheeseman;
5. U.S. Patent No. 5,599,675, issued February 4, 1997, Brenner;
6. U.S. Patent No. 5,654,419, issued August 5, 1997, Mathies;
7. U.S. Patent No. 5,728,528, issued March 17, 1998, Mathies;
8. U.S. Patent No. 5,763,594, issued June 9, 1998, Hiatt et al.;
9. U.S. Patent No. 5,770,367, issued June 23, 1998, Southern;
10. U.S. Patent No. 5,804,386, issued September 8, 1998, Ju;
11. U.S. Patent No. 5,808,045, issued September 15, 1998, Hiatt

Jingyue Ju et al.
Serial No.: 10/735,081
Filed: December 11, 2003
Page 21

et al.;

12. U.S. Patent No. 5,814,454, issued October 29, 1998, Ju;
13. U.S. Patent No. 5,834,203, issued November 10, 1998, Katzir;
14. U.S. Patent No. 5,849,542, issued December 15, 1998, Reeve et al.;
15. U.S. Patent No. 5,853,992, issued December 29, 1998, Glazer;
16. U.S. Patent No. 5,869,255, issued February 9, 1999, Mathies;
17. U.S. Patent No. 5,872,244, issued February 16, 1999, Hiatt et al.
18. U.S. Patent No. 5,876,936, issued December 29, 1999, Ju;
19. U.S. Patent No. 5,885,775, issued March 23, 1999, Haff et al.;
20. U.S. Patent No. 5,945,283, issued August 31, 1999, Kwok;
21. U.S. Patent No. 5,952,180, issued September 14, 1999, Ju;
22. U.S. Patent No. 6,028,190, issued February 28, 2000, Mathies;
23. U.S. Patent No. 6,046,005, issued April 4, 2000, Ju;
24. U.S. Patent No. 6,074,823, issued June 13, 2000, Hubert;

25. U.S. Patent No. 6,136,543, issued October 24, 2000, Anazawa et al.;
26. U.S. Patent No. 6,197,557, issued March 6, 2001, Markarov et al.;
27. U.S. Patent No. 6,214,987, issued April 10, 2001, Hiatt et al.;
28. U.S. Patent No. 6,218,118, issued April 17, 2001, Sampson;
29. U.S. Patent No. 6,218,530, issued April 17, 2001, Rothschild et al.;
30. U.S. Patent No. 6,232,465, issued May 15, 2001, Hiatt et al.;
31. U.S. Patent No. 6,312,893, issued November 6, 2001, Van Ness et al.;
32. U.S. Patent No. 6,316,230, issued November 13, 2001, Egholm;
33. U.S. Patent No. 6,361,940 issued March 26, 2002, Van Ness et al.;
34. U.S. Patent No. 6,613,508, issued September 2, 2003, Ness et al.;
35. U.S. Patent No. 6,627,748, issued September 30, 2003, Ju et al.;
36. U.S. Patent No. 6,664,079, issued December 16, 2003, Ju et

al.;

37. U.S. Patent No. 6,787,308, Balasubramanian et al., issued September 7, 2004;
38. U.S. Patent No. 6,833,246, issued to Balasubramanian et al. on December 21, 2004;
39. U.S. Patent No. 7,057,026, issued to Barnes et al. on June 6, 2006;
40. U.S. Patent No. 7,074,597, issued July 11, 2006, Ju;
41. U.S. Application Publication No. 2002/0168642 A1, published November 14, 2002 (Drukier);
42. U.S. Application Publication No. 2003/0008285 A1, published January 9, 2003 (Fischer);
43. U.S. Application Publication No. 2003/0022225 A1, published January 30, 2003 (Monforte et al.);
44. U.S. Application Publication No. 2003/0027140, published February 6, 2003 (Ju et al.);
45. U.S. Application Publication No. 2003/0044871, published March 6, 2003 (Cutsforth et al.);
46. U.S. Application Publication No. 2003/0099972, published May 29, 2003 (Olejnuk et al.);
47. U.S. Application Publication No. 2004/0185466, published September 23, 2004 (Ju et al.);

48. U.S. Application Publication No. 2005/0032081, published February 10, 2005 (Ju et al.);
49. U.S. Application Publication No. 2006/0057565, published March 16, 2006 (Ju et al.);
50. U.S. Application Publication No. 2006/0003352, published January 5, 2006 (Lipkin et al.);
51. PCT International Publication No. WO 91/06678, May 16, 1991 (**Exhibit 1**);
52. PCT International Publication No. WO 00/53805, September 14, 2000 (**Exhibit 2**);
53. PCT International Publication No. WO 01/92284, December 6, 2001 (**Exhibit 3**);
54. PCT International Publication No. WO 01/27625 A1, published April 19, 2001 (**Exhibit 4**);
55. PCT International Publication No. WO 02/079519 A1, published October 10, 2002 (**Exhibit 5**);
56. PCT International Publication No. WO 02/22883 A1, published March 21, 2002 (**Exhibit 6**);
57. PCT International Publication No. WO 02/29003, published April 11, 2002 (**Exhibit 7**);
58. PCT International Publication No. WO 04/007773, published January 22, 2004 (**Exhibit 8**);
59. PCT International Publication No. WO 04/055160, published

January 22, 2004 (**Exhibit 9**);

60. PCT International Publication No. WO 05/084367, published September 15, 2005 (**Exhibit 10**);
61. PCT International Publication No. WO 06/073436, published July 13, 2006 (**Exhibit 11**);
62. PCT International Publication No. WO 07/002204, published January 4, 2007 (**Exhibit 12**);
63. European Patent Application No. EP 0992511 A, Rapigene Inc., published April 12, 2000 (**Exhibit 13**);
64. Axelrod, V. D. et al. (1978) Specific termination of RNA polymerase synthesis as a method of RNA and DNA sequencing. *Nucleic Acids Res.* 5(10):3549-3563 (**Exhibit 14**);
65. Badman, E. R. et al. (2000) A Parallel Miniature Cylindrical Ion Trap Array. *Anal. Chem.* 72:3291-3297 (**Exhibit 15**);
66. Badman, E. R. et al. (2000) Cylindrical Ion Trap Array with Mass Selection by Variation in Trap Dimensions. *Anal. Chem.* 72:5079-5086 (**Exhibit 16**);
67. Benson, S. C., Mathies, R. A. and Glazer, A. N. (1993) Heterodimeric DNA-binding dyes designed for energy transfer: stability and applications of the DNA complexes. *Nucleic Acids Res.* 21:5720-5726 (**Exhibit 17**);
68. Benson, S. C., Singh, P. and Glazer, A. N. (1993) Heterodimeric DNA-binding dyes designed for energy

- transfer: synthesis and spectroscopic properties. *Nucleic Acids Res.* 21:5727-5735 (**Exhibit 18**);
69. Burgess, K. et al. (1997) Photolytic Mass Laddering for Fast Characterization of Oligomers on Single Resin Beads. *J. Org. Chem.* 62:5662-5663 (**Exhibit 19**);
70. Canard, B. et al. (1995) Catalytic editing properties of DNA polymerases. *Proc. Natl. Acad. Sci. USA* 92:10859-10863 (**Exhibit 20**);
71. Caruthers, M. H. (1985) Gene synthesis machines: DNA chemistry and its uses. *Science* 230:281-285 (**Exhibit 21**);
72. Chee, M. et al. (1996) Accessing genetic information with high-density DNA arrays. *Science* 274:610-614 (**Exhibit 22**);
73. Chen, X. and Kwok, P.-Y. (1997) Template-directed dye-terminator incorporation (TDI) assay: a homogeneous DNA diagnostic method based on fluorescence resonance energy transfer. *Nucleic Acids Res.* 25:347-353 (**Exhibit 23**);
74. Edwards, J. et al. (2001) DNA sequencing using biotinylated dideoxynucleotides and mass spectrometry. *Nucleic Acids Res.* 29(21):e104 (**Exhibit 24**);
75. Griffin, T. J. et al. (1999) Direct Genetic Analysis by Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry. *Proc. Nat. Acad. Sci. USA* 96:6301-6306 (**Exhibit 25**);
76. Hacia, J. G., Edgemon, K., Sun, B., Stern, D., Fodor, S. A., and Collins, F.S. (1998) Two Color Hybridization

- Analysis Using High Density Oligonucleotide Arrays and Energy Transfer Dyes. *Nucleic Acids Res.* 26:3865-6 (**Exhibit 26**);
77. Haff, L. A. et al. (1997) Multiplex Genotyping of PCR Products with Mass Tag-Labeled Primers. *Nucleic Acids Res.* 25(18):3749-3750;
78. Hyman, E. D. (1988) A new method of sequencing DNA. *Analytical Biochemistry* 174:423-436 (**Exhibit 27**);
79. Ireland, R. E. and Varney M. D. (1986) Approach to the total synthesis of chlorothricolide - synthesis of (+/-)-19.20-dihydro-24-O-methylchlorothricolide, methyl-ester, ethyl carbonate. *J. Org. Chem.* 51: 635-648 (**Exhibit 28**);
80. Jiang-Baucom, P. et al. (1997) DNA Typing of Human Leukocyte Antigen Sequence Polymorphisms by Peptide Nucleic Acid Probes and MALDI-TOF Mass Spectrometry. *Anal. Chem.* 69:4894-4896 (**Exhibit 29**);
81. Ju, J., Glazer, A. N. and Mathies, R. A. (1996) Energy transfer primers: A new fluorescence labeling paradigm for DNA sequencing and analysis. *Nature Medicine* 2:246-249 (**Exhibit 30**);
82. Ju, J., Ruan, C., Fuller, C. W., Glazer, A. N. and Mathies, R. A. (1995) Fluorescence energy transfer dye-labeled primers for DNA sequencing and analysis. *Proc. Natl. Acad. Sci. USA* 92:4347-4351 (**Exhibit 31**);
83. Kamal, A., Laxman, E., and Rao, N. V. (1999) A mild and

- rapid regeneration of alcohols from their allylic ethers by chlorotrimethylsilane/sodium iodide. *Tetrahedron Lett.* 40: 371-372 (**Exhibit 32**);
84. Lee, L. G. et al. (1992) DNA sequencing with dye-labeled terminators and T7 DNA polymerase: effect of dyes and dNTPs on incorporation of dye terminators and probability analysis of termination fragments. *Nucleic Acids Res.* 20:2471-2483 (**Exhibit 33**);
85. Lee, L. G. et al. (1997) New energy transfer dyes for DNA Sequencing. *Nucleic Acids Res.* 25:2816-2822 (**Exhibit 34**);
86. Li, J. (1999) Single Oligonucleotide Polymorphism Determination Using Primer Extension and Time-of-Flight Mass Spectrometry. *Electrophoresis*, 20:1258-1265 (**Exhibit 35**);
87. Liu, H. et al. (2000) Development of Multichannel Devices with an Array of Electrospray Tips for High-Throughput Mass Spectrometry. *Anal. Chem.* 72:3303-3310 (**Exhibit 36**);
88. Lyamichev, A. et al. (1999) Polymorphism Identification and Quantitative Detection of Genomic DNA by Invasive Cleavage of Oligonucleotide Probes. *Nat. Biotech.* 17:292-296 (**Exhibit 37**);
89. Metzker, M. L., et al. (1994) Termination of DNA synthesis by novel 3'-modified deoxyribonucleoside 5'-triphosphates. *Nucleic Acids Res.* 22:4259-4267 (**Exhibit 38**);
90. Olejnik, J., et al. (1995) Photocleavable biotin derivatives: a versatile approach for the isolation of biomolecules. *Proc. Natl. Acad. Sci. USA.* 92:7590-7594

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91. Pelletier, H., Sawaya, M. R., Kumar, A., Wilson, S. H., and Kraut J. (1994) Structures of ternary complexes of rat DNA polymerase β , a DNA template-primer, and ddCTP. *Science* 264:1891-1903 (Exhibit 40);
92. Prober, J. M., Trainor, G. L., Dam, R. J., Hobbs, F. W., Robertson, C. W., Zagursky, R. J., Cocuzza, A. J., Jensen, M. A., Baumeister K. (1987) A system for rapid DNA sequencing with fluorescent chain-terminating dideoxynucleotides. *Science* 238:336-341 (Exhibit 41);
93. Ronaghi, M., Uhlen, M., and Nyren, P. (1998) A sequencing Method based on real-time pyrophosphate. *Science* 281:364-365 (Exhibit 42);
94. Rosenblum, B. B. et al. (1997) New dye-labeled terminators for improved DNA sequencing patterns. *Nucleic Acids Res.* 25:4500-4504 (Exhibit 43);
95. Ross, P. et al. (1998) High Level Multiplex Genotyping by MALDI-TOF Mass Spectrometry. *Nat. Biotech.* 16:1347-1351 (Exhibit 44);
96. Ross, P. L. et al. (1997) Discrimination of Single-Nucleotide Polymorphisms in Human DNA Using Peptide Nucleic Acid Probes Detected by MALDI-TOF Mass Spectrometry. *Anal. Chem.* 69:4197-4202 (Exhibit 45);
97. Saxon, E. and Bertozzi, C. R. (2000) Cell surface engineering by a modified Staudinger reaction. *Science* 287:2007-2010 (Exhibit 46);

98. Schena, M., Shalon, D., Davis, R., and Brown, P. O. (1995) Quantitative monitoring of gene expression patterns with a complementary DNA microarray. *Science* 270:467-470 (**Exhibit 47**);
99. Speicher, M. R., Ballard, S. G. and Ward, D. C. (1996) Karyotyping human chromosomes by combinatorial multi-fluor FISH. *Nature Genetics* 12:368-375 (**Exhibit 48**);
100. Stoerker, J. et al. (2000) Rapid Genotyping by MALDI-monitored nuclease selection from probe libraries. *Nat. Biotech.* 18:1213-1216 (**Exhibit 49**);
101. Welch, M. B., and Burgess, K. (1999) Synthesis of fluorescent, photolabile 3'-O-protected nucleoside triphosphates for the base addition sequencing scheme. *Nucleosides and Nucleotides* 18:197-201 (**Exhibit 50**);
102. Woolley, A. T. et al. (1997) High-Speed DNA Genotyping Using Microfabricated Capillary Array Electrophoresis Chips. *Anal. Chem.* 69:2181-2186 (**Exhibit 51**);
103. Fei, Z. et al. (1998) MALDI-TOF mass spectrometric typing of single nucleotide polymorphisms with mass-tagged ddNTPs. *Nucleic Acids Research* 26(11):2827-2828 (**Exhibit 52**);
104. Olejnik, J. et al. (1999) Photocleavable peptide-DNA conjugates: synthesis and applications to DNA analysis using MALDI-MS. *Nucleic Acids Res.* 27(23):4626-4631 (**Exhibit 53**);
105. Arbo, et al. (1993) Solid Phase Synthesis of Protected Peptides Using New Cobalt (III) Amine Linkers, *Int. J.*

Peptide Protein Res. 42:138-154 (**Exhibit 54**);

106. Chiu, N.H., Tang, K., Yip, P., Braun, A., Koster, H., and Cantor C.R.(2000) Mass spectrometry of single-stranded restriction fragments captured by an undigested complementary sequence. *Nucleic Acids Res.* 28:E31 (**Exhibit 55**);
107. Fu, D. J., Tang, K., Braun, A., Reuter, D., Darnhofer-Demar, B., Little D. P., O'Donnell, M. J., Cantor, C.R., and Koster, (1998) Sequencing exons 5 to 8 of the p53 gene by MALDI-TOF mass spectrometry. *Nat. Biotechnol.* 16:381-384 (**Exhibit 56**);
108. Monforte, J. A., and Becker, C. H. (1997) High-throughput DNA analysis by time-of-flight mass spectrometry. *Nat. Med.* 3(3):360-362 (**Exhibit 57**);
109. Roskey, M. T, Juhasz P., Smirnov, I. P., Takach, E.J., and Martin, S.A. (1996) Haff L.A., DNA sequencing by delayed extraction-matrix-assisted laser desorption/ionization time of flight mass spectrometry. *Proc. Natl. Acad. Sci. USA.* 93:4724-4729 (**Exhibit 58**);
110. Tang, K., Fu, D. J., Julien, D., Braun, A., Cantor, C. R., and Koster H. (1999) Chip-based genotyping by mass spectrometry. *Proc. Natl. Acad. Sci. USA.* 96:10016-10020 (**Exhibit 59**);
111. Tong, X. and Smith L. M. (1992) Solid-Phase Method for the Purification of DNA Sequencing Reactions. *Anal. Chem.* 64: 2672-2677 (**Exhibit 60**);
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- Jacob, A, Koster, H., (1997) Recovery of nucleic acids from immobilized biotin-streptavidin complexes using ammonium hydroxide and application in MALDI-TOF mass spectrometry. *Anal. Chem.* 69:904-910 (**Exhibit 61**);
113. Jingyue Ju, et al., (1996) "Cassette labeling for facile construction of energy transfer fluorescent primers", *Nuc. Acids Res.* 24(6):1144-1148 (**Exhibit 62**);
114. Bergseid M., Baytan A.R., Wiley J.P., Ankener W.M., Stolowitz, Hughs K.A., Chestnut J.D., (2000) "Small-molecule base chemical affinity system for the purification of proteins", *BioTechniques* 29:1126-1133 (**Exhibit 63**);
115. Speicher, M. R., Ballard, S. G. and Ward, D. C., (1996) "Karyotyping human chromosomes by combinatorial multi-fluor FISH". *Nature Genetics* 12:368-375 (**Exhibit 64**);
116. Hultman et al., (1989) "Direct Solid Phase Sequencing of Genomic and Plasmid DNA Using Magnetic Beads as Solid Support", *Nucleic Acids Research*, 17(3):4937-4946 (**Exhibit 65**);
117. Ikeda, K. et al., (1995) "A Non-Radioactive DNA Sequencing Method Using Biotinylated Dideoxynucleoside Triphosphates and Delta TTH DNA Polymerase" *DNA Research*, 2(31):225-227 (**Exhibit 66**);
118. Kim Sobin et al., (2002) "Solid Phase Capturable Dideoxynucleotides for Multiplex Genotyping Using Mass Spectrometry" *Nucleic Acids Research*, 30(16):e85.1-e85.6 (**Exhibit 67**);
119. Supplementary European Search Report issued February 16,

- 2004 in connection with European Patent Application No. 01 97 7533 (**Exhibit 68**);
120. Supplementary European Search Report issued February 9, 2007 in connection with European Patent Application No. 03 76 4568.6 (**Exhibit 69**);
121. Supplementary European Search Report issued May 25, 2005 in connection with European Patent Application No. 02 72 8606.1 (**Exhibit 70**);
122. Supplementary European Search Report issued June 7, 2005 in connection with European Patent Application No. 01 96 8905 (**Exhibit 71**);
123. International Preliminary Examination Report issued on 3/18/05 in connection with PCT/US03/21818 (**Exhibit 72**);
124. International Preliminary Examination Report issued on 4/3/03 in connection with PCT/US01/31243 (**Exhibit 73**);
125. International Preliminary Examination Report issued on 2/25/03 in connection with PCT/US01/28967 (**Exhibit 74**);
126. International Preliminary Examination Report issued on 3/17/03 in connection with PCT/US02/09752 (**Exhibit 75**);
127. International Preliminary Report on Patentability issued on 9/5/06 in connection with PCT/US05/006960 (**Exhibit 76**);
128. International Search Report issued 5/13/02 in connection with PCT/US01/31243 (**Exhibit 77**);
129. International Search Report issued 1/23/02 in connection with PCT/US01/28967 (**Exhibit 78**);

130. International Search Report issued 9/18/02 in connection with PCT/US02/09752 (**Exhibit 79**);
131. International Search Report issued 9/26/03 in connection with PCT/US03/21818 (**Exhibit 80**);
132. International Search Report issued 6/8/04 in connection with PCT/US03/39354 (**Exhibit 81**);
133. International Search Report issued 11/4/05 in connection with PCT/US05/06960 (**Exhibit 82**);
134. International Search Report issued 12/15/06 in connection with PCT/US05/13883 (**Exhibit 83**);
135. Written Opinion of the International Searching Authority issued 10/27/05 in connection with PCT/US05/06960 (**Exhibit 84**);
136. Written Opinion of the International Searching Authority issued 12/15/06 in connection with PCT/US05/13883 (**Exhibit 85**);
137. Elango, N. et al. (1983) "Amino Acid Sequence of Human Respiratory Syncytial Virus Nucleocapsid Protein" Nucleic Acids Research, 11(17):5941-5951 (**Exhibit 86**);
138. Buck, G.A. et al. (1999) "Design Strategies and Performance of Custom DNA Sequencing Primers", BioTechniques, 27(3):528-536 (**Exhibit 87**);
139. Hafliger, D. et al. (1997) "Seminested RT-PCR Systems for Small Round Structured Viruses and Detection of Enteric

Viruses in Seafood", International Journal of Food Microbiology, 37:27-36 (**Exhibit 88**);

140. Leroy, E.M. et al. (2000) "Diagnosis of Ebola Haemorrhagic Fever by RT-PCR in an Epidemic Setting", Journal of Medical Virology, 60:463-467 (**Exhibit 89**);
141. Kokoris, M. et al. (2000) "High-throughput SNP Genotyping With the Masscode System", Molecular Diagnosis, 5(4):329-340 (**Exhibit 90**);
142. Kim, S. et al. (2003) "Multiplex Genotyping of the Human β 2-adrenergic Receptor Gene Using Solid-phase Capturable Dideoxynucleotides and Mass Spectrometry", Analytical Biochemistry, 316:251-258 (**Exhibit 91**);
143. Haff, L. A. et al. (1997) Multiplex Genotyping of PCR Products with Mass Tag-Labeled Primers. *Nucleic Acids Res.* 25(18):3749-3750 (**Exhibit 92**);
144. PCT International Publication No. WO/2004/018493, Solexa Ltd., March 4, 2004 (**Exhibit 93**); and
145. PCT International Publication No. WO/2004/018497, Solexa Ltd., March 3, 2004 (**Exhibit 94**).

This Supplemental Information Disclosure Statement is being submitted under 37 C.F.R. §1.97(c)(2). Accordingly, applicants enclose herewith a check for ONE HUNDRED AND EIGHTY DOLLARS (\$180.00). Applicants request that the Examiner review the items listed and make them of record in the subject application.

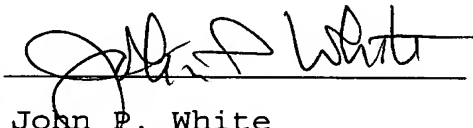
If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned

Jingyue Ju et al.
Serial No.: 10/735,081
Filed: December 11, 2003
Page 36

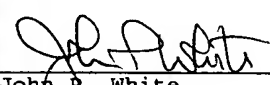
attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed total fee of \$690.00 fee, including a \$180.00 fee for filing a Supplemental Information Disclosure Statement and \$510.00 fee for a three-month extension of time is deemed necessary in connection with the filing of this Amendment and Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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